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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,500	03/11/2005	Jesus G Valenzuela	4239-66903-02	9994

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EXAMINER	
ARCHIE, NINA	
ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,500	VALENZUELA ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-6,25,27-33,35,36 and 77-89* is/are pending in the application.

4a) Of the above claim(s) *27-33,35,36 and 82-89* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,5,6,25,77-79 and 81* is/are rejected.

7)☒ Claim(s) *3-4, and 80* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office is responsive to Applicant's amendment and response filed 2-11-08. Claims 2-4, 6, 25, 27, 33, 35, and 36 have been amended. Claims 1, 7-24, 26, 34, and 37-76 have been cancelled. Claims 27-33, 35-36 have been withdrawn from consideration. Claims 77-89 are new claims.

Election/Restriction

2. As set forth in the restriction made on 6/15/2007, there was a lack of unity. Therefore since the newly submitted clams 82-89, drawn to a method are distinct from examined claims 1-7 and 25 drawn to a polypeptide, antigenic fragment, and pharmaceutical composition, that has been elected. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 82-89 are withdrawn from consideration as being directed to a non-elected invention.

Rejections Withdrawn

3. In view of the Applicant's amendment and remark following rejections are withdrawn.

a) Rejection of claim 1 under 35 U.S.C. 102 (b) is withdrawn in light of applicant's amendment of the claims.

Rejection Maintained

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The rejection of claims 2, 5-6, and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained for the reasons set forth in the previous office action.

Applicant arguments:

As established in Ex parte Parks, "adequate description under the first paragraph of 35 U.S.C. 112 does not require literal support for the claimed invention ....Rather, it is sufficient if the originally-filed disclosure would have conveyed to one having ordinary skill in the art that an appellant had possession of the concept of what is claimed" Exparte Parks, 30 USPQ2d 1234, 1236-37 (B.P.A.I. 1993) (emphasis added). Moreover, the MPEP at §2163 states that "[w]hat is conventional or well known to one of skill in the art need not be disclosed in detail. See Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d at 1384,231 USPQ at 94. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. See, e.g. Vas-Cath, 935 F.2d at 1563, 19 USPQ2d at 1116; Martin v. Johnson, 454 F.2d 746, 751,172 USPQ 391,395 (CCPA 1972) (stating "description need not be in ipsis verbis [i.e., "in the same words"] to be sufficient")."

In the current instance, the original disclosure clearly conveys that Applicants had possession of the claimed invention, and certainly of the concept of what is currently claimed.

Applicants had possession of the peptide sequence set forth in SEQ ID NO: 11. Applicants had also contemplated and provided explicit written description of polypeptides comprising at least 95% sequence identity to SEQ ID NO: 11 (specification, for example, at page 22, lines 21-23; page 35, lines 24-

27), conservative variants of SEQ ID NO: 11 (for example, at page 10, line 26 through page 11, line 29), and immunogenic fragments comprising at least fifteen consecutive amino acids of SEQ ID NO: 11 (for example, at page 36, lines 5-7). The Office action alleges that in order to "adequately describe the genus of the amino acid of SEQ ID NO: 11, applicant must also give a functional limitation of amino acid SEQ ID NO: 11" (Office action at page 5). Applicants respectfully submit that the claims, in fact, require that the polypeptide produce an immune response to P. ariasi in a subject. Thus, the claims do include a functional limitation.

Applicants also note that alignment methods are provided for identifying the claimed variants of SEQ ID NO: 11 (for example, at page 21, line 21 through page 22, line 31) and the specification describes that the claimed polypeptides can be purified and sequenced using standard techniques (for example, at page 20, lines 4-8, page 36, line 24 through page 37, line 3). Methods are also provided for identifying sequence variants having the claimed activity (for example, at page 13, line 26 through page 14, line 1; page 79, line 18 through page 100, line 19). Thus, the specification provides sufficient written description to convey to one of skill in the art that the inventors had possession of the claimed polypeptides at the time the application was filed.

The Office is reminded that the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. Guidelines for Examination of Patent Applications under the 35 U.S.C. § 112, q[1, "Written Description" Requirement 66 Fed. Reg. 1099, 1106 (2001). Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that Applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. Id. Applicants submit that the knowledge and level of skill in the art would allow a person of ordinary skill to envision the claimed sequences based on the teachings of the specification, the provision of SEQ ID

NO: 11 itself, and its activity (producing an immune response to P. ariasi in a subject). As claims 2, 5, 6, and 25 are sufficiently described by the specification, Applicants request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

Examiner's Response to Applicant's Arguments:

Examiner accepts that the claims have been amended. Examiner accepts that the original disclosure clearly conveys that Applicants had possession of the claimed invention, and certainly of the concept of what is currently claimed.

Applicants had possession of the peptide sequence set forth in SEQ ID NO: 11. Applicants had also contemplated and provided explicit written description of polypeptides comprising at least 95% sequence identity to SEQ ID NO: 11 (specification, for example, at page 22, lines 21-23; page 35, lines 24-27), conservative variants of SEQ ID NO: 11 (for example, at page 10, line 26 through page 11, line 29), and immunogenic fragments comprising at least fifteen consecutive amino acids of SEQ ID NO: 11 (for example, at page 36, lines 5-7). The Office action alleges that in order to "adequately describe the genus of the amino acid of SEQ ID NO: 11, applicant must also give a functional limitation of amino acid SEQ ID NO: 11" (Office action at page 5). Applicants respectfully submit that the claims, in fact, require that the polypeptide produce an immune response to P. ariasi in a subject. Thus, the claims do include a functional limitation.

The specification, however, does not disclose distinguishing and identifying features of a representative member of the genus of the amino acids of SEQ ID NO:11 to which the claims are drawn, such as a correlation between structure of the peptide and its recited function, so that the skilled artisan could immediately envision or recognize at least a substantial number of members of the claimed genus of antigens.

MPEP § 2163.02 states, "an objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she

invented what is claimed". The courts have decided: The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. See Vas-Cath, Inc.'v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993)and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "'Written Description" Requirement (66 FR 1099-1111, January 5,2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104).

The Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome and form immunoepitopes. Bowie et al. further teach that the

problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). Additionally as evidenced by Greenspan et al. (Nature Biotechnology 7: 936-937, 1999), defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, Or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that can elicit a protective immune response to a given pathogen can only be identified empirically. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of immunoepitopes, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of antigens. Therefore, in accordance with the Guidelines, the description of amino acid is not deemed representative of the genus amino acid of SEQ ID NO: 11 of the claim invention thus the claim does not meet the written description requirement.

New Grounds of Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear,

concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 25 and 81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an immunogenic composition, does not reasonably provide enablement for a pharmaceutical composition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claimed invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

(A) The breadth of the claims;
(B)The nature of the invention;
(C)The state of the prior art;
(D)The level of one of ordinary skill;
(E)The level of predictability in the art;
(F)The amount of direction provided by the inventor;
(G)The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims. The claims are broadly drawn to a pharmaceutical composition, comprising a therapeutically effective amount of the polypeptide and a pharmaceutically acceptable carrier. The quantity of experimentation required to practice the invention as claimed would require in vivo studies and in

vitro studies of the pharmaceutical composition, and further whereby treatment effects are provided for the claimed conditions. Since the specification fails to provide particular guidance for a pharmaceutical composition, comprising a therapeutically effective amount of the, it would require undue experimentation to practice the invention over the broad scope as presently claimed.

Nature of the invention. The claims are broadly drawn to a pharmaceutical composition, comprising a therapeutically effective amount of the polypeptide and a pharmaceutically acceptable carrier.

The state of the prior art. The art as at the time of filing teaches that: Although many investigators have tried to develop vaccines based on specific antigens, it is well understood that the ability of an antigen to stimulate antibody production does not necessarily correlate with the ability of the antigen to stimulate an immune response capable of protecting an animal from infection (Chandrashekar et al., US Patent 6,248,329, col. 1, lines 35-41). It is well recognized in the vaccine art, that it is unclear whether an antigen derived from a pathogen will elicit protective immunity. Ellis (Chapter 29 of Vaccines, Plotkin, et al. (eds) WB Saunders, Philadelphia, 1998, especially p. 571, paragraph 2) exemplifies this problem in the recitation that "the key to the problem (of vaccine development) is the identification of that protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies.., and thus protect the host against attack by the pathogen. Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome and form immunoepitopes. Bowie et al. further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural

determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). Therefore the state of the art questions the a pharmaceutical composition as claimed as set forth supra and can treat all opportunistic infections and severe diseases. For the reasons set forth supra, the state of the art is has limitations to a pharmaceutical composition comprising the claimed invention as set forth supra.

Guidance in the specification. The specification discloses in Example 3 DNA Vaccination in Mice whereby, mice were inoculated in the P. ariasi and the response was measured 24 hours after the injection by measuring thickness and and redness of ear. Example 4 discloses the production of an immune response in dogs with natural immunity against the leishmaniasis in order to determine which P. ariasi salivary gland proteins are recognized by a protective immune response. However, one skilled in the art would not accept on its face the examples given in the specification as being correlative or representative of a successful pharmaceutical composition in view of the of general guidance in the specification of an immunogenic composition that is capable of generating an immune response. The specification gives in vivo examples administering an immunogenic composition and not a pharmaceutical composition. Therefore, the specification as filed fails to provide particular guidance demonstrating a reasonable extrapolation.

Working examples. The specification provides working examples to the subject matter being sought in the claims in the context of an immunogenic composition not a pharmaceutical composition as claimed.

In conclusion, the claimed inventions are not enabled for any pharmaceutical composition only an immunogenic composition. The claims are broadly drawn to a pharmaceutical composition, comprising a therapeutically effective amount of the polypeptide and a pharmaceutically acceptable carrier. The art as at the time of filing teaches that: Although many investigators have tried to develop vaccines based on specific antigens, it is well understood that the ability of an antigen to stimulate antibody production does not necessarily correlate with the ability of the antigen to stimulate an immune response capable of protecting an animal from infection and it is well recognized in the vaccine art, that it is unclear whether an antigen derived from a pathogen will elicit protective immunity thus the state of the art is unpredictable. As a result, for the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 2, 5-6, 77-79 are rejected under 35 U.S.C. 102(b) as being anticipated by Jacobs et al WO9920644 Date April 29, 1999.

Claims 2, 6, and 77-79 are drawn to a substantially purified salivary *P. ariasi* polypeptide.

Jacobs et al teach an antigenic fragment of the polypeptide of SEQ ID NO: 11 (see STIC RESULTS).

Status of the Claims

8. Claims 2, 5-6, 25, and 77-79 and 81 are rejected.

Claims 3-4, and 80 are objected as being dependent from a base claim.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public

PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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